Predictors of long-term patient survival after in situ vein leg bypass

Peter G. Kalman, MD, FRCSC, and **K. Wayne Johnston, MD, FRCSC,**
Toronto, Ontario, Canada

Purpose: **The objective was to determine the long-term survival rates of patients who undergo distal arterial bypass surgery and to identify the preoperative factors that are predictive of survival.**
Methods: **Three hundred fifty-eight consecutive in situ distal leg bypass procedures were performed between July 1986 and December 1995. The relationship between 13 preoperative variables and late survival were determined using both univariate (Kaplan-Meier) and multivariate (Cox regression) statistical techniques.**
Results: **The cumulative survival rates at 1, 3, 5, and 7 years were 86.6% ± 2.0%, 63.2% ± 3.0%, 46.9% ± 3.4%, and 35.3% ± 3.8%, respectively. Using Cox regression, four significant variables were found to be associated with lower late survival rates: male gender, diabetes, chronic renal insufficiency (patients with creatinine levels greater than or equal to 1.7 mg/dl or 150 SI units), and a history of cerebrovascular disease ($p <$ 0.001 for model). When none of these four variables were present, the predicted 5-year survival rate was 71%, whereas the survival rate was reduced to 43% to 60% when one was present, 23% to 42% when two were present, 8% to 22% when three were present, and 2% when all four were present.**
Conclusions: **This study defines the long-term survival rates in a cohort of patients after undergoing distal bypass surgery and demonstrates that certain preoperative factors are predictive of late survival. Knowledge of these factors may be useful to assist in individual operative decisions between aggressive attempts at distal revascularization versus primary amputation. (J Vasc Surg 1997;25:899-904.)**

The long-term patency rates for autologous saphenous vein distal bypass grafts are well established, and most patients who have an appropriate indication are considered suitable surgical candidates.[1-6] The cost of treating patients who have critical ischemia, particularly with respect to the use of hospital resources, is significant.[7-9] Most notable is the impact on length of stay.[10] The current emphasis on cost containment has underscored the importance of achieving not only long-term graft patency but also maintaining or improving function. Unfortunately, there is sparse surgical literature that addresses the endpoints of functional outcome. Using the RAND 36-Item Health Survey, Duggan et al.[11] found that the functional scores of patients who underwent amputation were not significantly different from those who underwent successful revascularization procedures; hence, primary amputation may be an option for patients who have a short life expectancy or are not likely to achieve a good functional result.

Thus, in addition to considering technical success and functional outcome, long-term patient survival rates are also an important consideration during preoperative decisionmaking. The purpose of this paper was to determine the late survival rate of a large, consecutive cohort of patients who underwent arterial bypass procedures with in situ vein grafts and, using multivariate analysis, to determine the preoperative variables that predict long-term survival.

METHODS

Demographic data and outcome variables were collected prospectively in a consecutive group of pa-

From the Toronto Hospital Vascular Centre, and Division of Vascular Surgery, University of Toronto.
Reprint requests: Dr. Peter G. Kalman, The Toronto Hospital-General Division, Eaton Building 5EC-307, 200 Elizabeth St., Toronto, Ontario, Canada M5G 2C4.

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Table I. Demographic data for 358 consecutive patients who underwent in situ bypass

Age	
mean ± SD	68 ± 10 years
median	69 years
Gender	68% male
	32% female
Smoking history (past 10 years)	68%
Diabetes	38%
Coronary disease (history of MI, angina, CHF)	47%
Cerebrovascular disease (history of TIA, stroke)	20%
Pulmonary disease (COPD, $pCO_2 > 50$, $pO_2 < 60$)	12%
Renal insufficiency	12%
Prior ipsilateral surgery	20%
Indication:	
grade 0 (popliteal aneurysm)	1%
grade 1 (claudication)	20%
grade 2 (ischemic rest pain)	39%
grade 3 (ulcer, gangrene)	40%
Timing:	
elective	92%
emergency	8%
Proximal anastomosis:	
common femoral	55%
superficial femoral	33%
profunda	2%
proximal inflow graft	10%
Distal anastomosis:	
below knee popliteal	32%
tibial	68%
inframalleolar	30%
Mean preoperative ABI	0.35 ± 0.21
Mean postoperative ABI	0.84 ± 0.34

MI, Myocardial infarction; *CHF,* congestive heart failure; *TIA,* transient ischemic attack; *COPD,* chronic obstructive pulmonary disease; *ABI,* ankle-brachial index.

Table II. Perioperative morbidity and mortality data

Mortality rate (n = 4, all cardiac)	1.1%
Myocardial infarct (major)	5.0%
Stroke or TIA	1.7%
Hemorrhage/hematoma not requiring surgery	3.7%
Lymphocele/lymph leak	4.3%
Wound infection	20.7%
superficial	12.3%
deep	8.4%

TIA, Transient ischemic attack.

Table III. Incidence of late death of distal bypass group compared with Canadian population[23]

Cause	*Distal bypass*	*Canadian population*
Cardiovascular Disease	70.8%	39%
Cardiac	62.6%	
Stroke	8.2%	
Pulmonary	4.0%	8%
Renal	8.2%	
Malignancy	10.2%	28%
Other	6.8%	

tients who underwent in situ vein leg bypass procedures. These variables were defined according to the criteria prepared by the Ad Hoc Committee on Reporting Standards.[12] Postoperative follow-up (clinical and vascular laboratory surveillance) was conducted every 3 months during the first postoperative year and every 6 months thereafter. Graft patency was determined at each visit, and survival status and cause of death was determined by contact with the referring physician or family. The angiographic runoff score (Ad Hoc Committee on Reporting Standards[12]) ranges from 1 (best runoff) to 10 (worst runoff). For subgroup analysis, the median runoff score was determined (runoff score, 5), and patients were categorized as poor runoff (score ≥ 5) and good runoff (score < 5).

Cumulative graft patency and patient survival rates were determined using the Kaplan-Meier method.[13,14] The relationship between 13 preoperative variables and survival was analyzed using both univariate (Kaplan-Meier) and multivariate (Cox regression) statistical techniques. For each variable, the Kaplan-Meier method was used to determine the cumulative survival rate and the log-rank test (Mantel) was used to specify statistical differences between the subgroups.[15] The stepwise Cox proportional hazards model was used for the multivariate analysis of the preoperative factors that were predictive of late survival.[16] For comparison, survival data were obtained from published life tables for the age and gender–matched Ontario population.[17,18]

RESULTS

Three hundred fifty-eight in situ vein leg bypass procedures (116 [32%] below-knee femoropopliteal and 242 [68%] tibial bypass) were performed at the Toronto Hospital between July 1, 1986, and December 31, 1995. They represented 56% of our infrainguinal bypass procedures (autogenous and prosthetic) performed during this time period. There were also 140 procedures (22%) performed with reversed or nonreversed saphenous vein grafts and 138 (22%) with polytetrafluoroethylene (PTFE) grafts. This article reports the prospective data collected for the patients who underwent in situ bypass procedures because we have had a particular interest in the

Table IV. Preoperative variables and association with long-term survival (Kaplan-Meier) by univariate analysis

Variable	*p*
Gender (male vs female)	0.035
Surgeon (n = 4)	0.001
Timing of surgery (elective vs emergency)	0.935
Diabetes (IDDM or NIDDM vs nil)	0.001
Smoking history (within past 10 years vs nil)	0.136
Coronary artery disease (MI, angina, CHF vs nil)	0.004
Cerebrovascular disease (past TIA, stroke vs nil)	0.002
Respiratory disease (COPD vs nil)	0.565
Renal insufficiency (abnormal creatinine vs nil)	0.001
Indication for surgery (critical ischemia vs nil)	0.037
Previous vascular reconstruction (yes vs no)	0.074
Distal anastomosis (popliteal vs tibial)	0.048
Runoff index < 5 (i.e. median index; yes vs no)	0.094

Differences between variable subgroups determined by log-rank test (Mantel). Those variables with a *p* value less than 0.10 were selected in a stepwise fashion for inclusion into the multivariate model.
IDDM, Insulin-dependent diabetes mellitus; *NIDDM,* non–insulin-dependent diabetes mellitus; *MI,* myocardial infarction; *CHF,* congestive heart failure, *TIA,* transient ischemic attack; *COPD,* chronic obstructive pulmonary disease.

Table V. Independent predictors of long-term survival

Covariate	*Coefficient*	*SD*	*p*
Gender (male = 1; female = 0)	0.545	0.193	0.005
Diabetes (yes = 1; no = 0)	0.537	0.171	0.002
Renal insufficiency (creatinine > 1.7 mg%) (yes = 1; no = 0)	0.906	0.231	0.001
History of cerebrovascular disease (yes = 1; no = 0)	0.387	0.196	0.048

Variables with a *p* value < 0.10 with the univariate analysis were selected in a stepwise fashion for inclusion into the multivariate Cox regression model ($p = 0.001$ for model).

in situ technique and have followed the demographic and operative results in this subgroup in a prospective fashion. The reversed vein, nonreversed vein, and PTFE bypass grafts have not been observed in a similar fashion.

The demographic data are summarized in Table I, and the perioperative morbidity and mortality data are summarized in Table II.

Secondary patency and late survival data. The cumulative secondary patency rates at 1, 3, 5, and 7 years were 85.0% ± 1.9%, 81.4% ± 2.2%, 78.4% ± 2.6%, and 78.4% ± 2.6%, respectively. There were four deaths in the perioperative period (within 30 days of surgery or during the hospital admission), for an operative mortality rate of 1.1%.

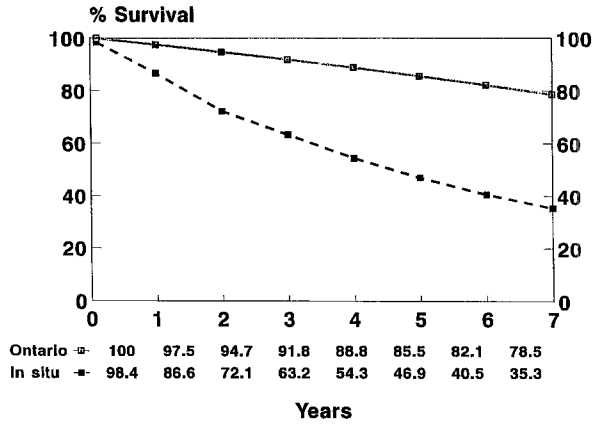

Fig. 1. Cumulative survival data of patients who underwent in situ bypass grafts, and comparison with age and gender–matched Ontario population.

The causes for late death are summarized in Table III. The most common cause was a cardiac event (62.6%). The cumulative survival rates at 1, 3, 5, and 7 years were 86.6% ± 2.0%, 63.2% ± 3.0%, 46.9% ± 3.4%, and 35.3% ± 3.8%, respectively (Fig. 1). The cumulative survival rate of these patients was significantly lower ($p < 0.001$) than the age and gender–matched Ontario population for the same time period (Fig. 1).

Preoperative factors associated with late survival. The significant variables associated with late survival and their *p* values are summarized in Table IV. Using stepwise multivariate analysis (Cox regression), the independent predictors for late survival were determined. As listed in Table V, there were four significant variables associated with lower late survival rates: male gender, diabetes, chronic renal insufficiency, and a history of cerebrovascular disease ($p < 0.001$ for model). The predicted survival rates for these four variables are shown in Fig. 2, *A* to *D*. Table VI and Fig. 3 summarize the predicted survival rates for the 16 combinations of the variables. Note that when none of these variables were present, the predicted 5-year survival rate was 71%, whereas the survival rate was reduced to 43% to 60% when one was present, 23% to 42% when two were present, 8% to 22% when three were present, and 2% when all four were present.

DISCUSSION

Meticulous operative techniques combined with postoperative graft surveillance are the two main factors that are responsible for the improvement in long-term patency rates after both in situ and re-

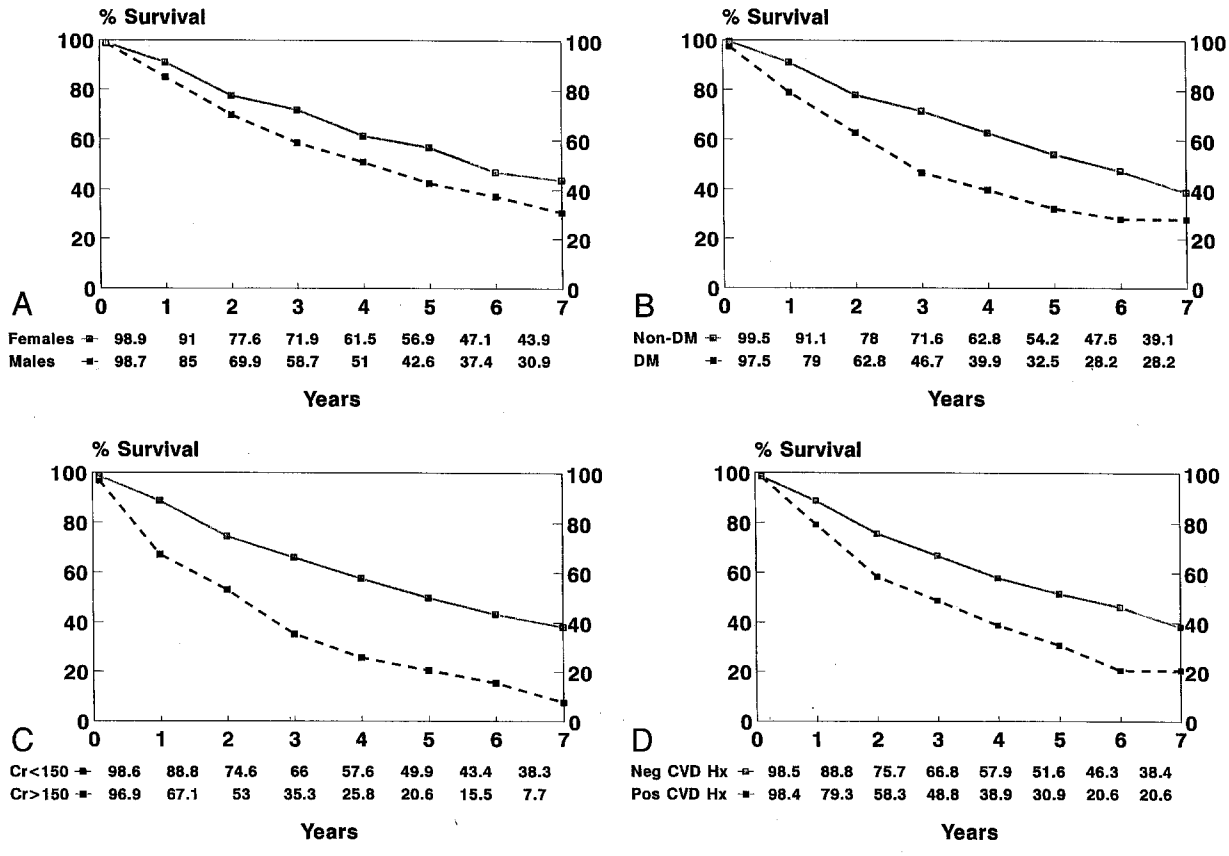

Fig. 2. Independent predictors of long-term survival: **A,** gender; **B,** diabetes; **C,** renal insufficiency (patients with creatine levels < or >1.7 mg/dl); **D,** history of cerebrovascular disease.

versed saphenous vein bypass grafts.[1-6] Although some believe that all patients who have critical limb ischemia should undergo an attempt at revascularization, in the present climate of cost containment other factors must be considered in addition to operability by angiographic criteria.[7-8,10] The decision for primary amputation is only straightforward when faced with a patient who has extreme cardiac, respiratory, or cerebrovascular disease, or whose poor cognitive status dictates only palliation of rest pain or distal infection. Although there are several reports that summarize technical success, there are few references in the surgical literature that deal with functional outcome after infrainguinal bypass surgery. Duggan and associates[11] evaluated the functional outcomes of limb salvage surgery by administering the RAND 36-Item Health Survey as a health assessment tool. Although they reported an 80% limb salvage rate, only 50% of patients survived at 3 years and only 25% survived with the salvaged extremity and were ambulatory. This finding clearly emphasizes that patency alone is an inadequate endpoint for operative success and that more information is necessary to help with our preoperative decisionmaking.

In patients who undergo infrainguinal bypass grafting procedures, the likelihood of long-term survival may be important in the preoperative decision process of certain individual patients. In recent reports, the 5-year survival rate has ranged from 38% to 66%, with death most commonly a result of coronary or cerebrovascular disease.[19-22] The cumulative 5- and 7-year survival rates in our entire cohort of patients were 46.9% ± 3.4% and 35.3% ± 3.8%, respectively. The detailed multivariate analysis was conducted to determine which variables, alone or in combination, would be useful in estimating late survival rates. The four significant independent predictors were male gender, diabetes, chronic renal insufficiency, and a history of cerebrovascular disease. We recognize the possibility of bias because of the inclusion of only patients who underwent in situ vein bypass grafting procedures, and we caution the

Table VI. Predicted 1 and 5-year survival data for all combinations of significant variables by Cox regression

				Cumulative survival rates	
A	*B*	*C*	*D*	*1 year*	*5 years*
F	no	no	no	94.3 ± 0.2%	70.8 ± 0.7%
F	no	no	yes	91.7 ± 0.3%	60.1 ± 1.0%
F	yes	no	no	90.5 ± 0.3%	55.4 ± 1.2%
M	no	no	no	90.4 ± 0.3%	55.1 ± 1.2%
F	no	yes	no	86.5 ± 0.4%	42.5 ± 1.7%
F	yes	no	yes	86.3 ± 0.4%	41.9 ± 1.7%
M	no	no	yes	86.2 ± 0.5%	41.6 ± 1.7%
M	yes	no	no	84.1 ± 0.5%	36.1 ± 2.0%
F	no	yes	yes	80.8 ± 0.6%	28.4 ± 2.5%
F	yes	yes	no	78.1 ± 0.8%	23.2 ± 2.9%
M	no	yes	no	77.9 ± 0.8%	22.9 ± 2.9%
M	yes	no	yes	77.5 ± 0.8%	22.3 ± 3.0%
F	yes	yes	yes	69.4 ± 1.1%	11.6 ± 4.3%
M	no	yes	yes	69.2 ± 1.1%	11.4 ± 4.3%
M	yes	yes	no	65.2 ± 1.3%	8.0 ± 5.0%
M	yes	yes	yes	53.3 ± 1.9%	2.4 ± 7.3%

A, Gender; *B,* diabetes; *C,* creatinine level 1.7 mg/dl or greater; *D,* history of cerebrovascular disease.

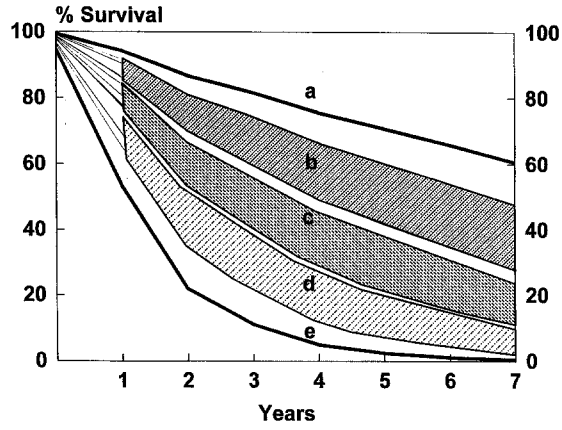

Fig. 3. Cumulative survival data (Cox regression) for all combinations of significant variables (*a,* four variables absent; *b,* one variable present; *c,* two variables present; *d,* three variables present; *e,* four variables present).

reader that the results may not be generalizable to patients who are undergoing reversed or nonreversed vein bypass or prosthetic bypass.

In our patients, men had significantly lower 5- and 7-year survival rates when compared with women (42.6% ± 4.1% and 30.9% ± 4.6% vs 56.9% ± 6.2% and 43.9% ± 7.1%, respectively). This gender relationship is in keeping with the higher annual mortality rate observed in men from all cardiovascular diseases in an age-standardized Canadian population.[23,24] In men, the annual mortality rate that resulted from cardiovascular disease was 315 per 100,000 per year, compared with 187 per 100,000 per year for women.[23,24] Our results are in contrast to a previous study by Magnant and associates,[25] where the survival rate at 3 years was 54% in women and 72% in men. Our 3-year survival rate was 72% in women compared with 59% in men. The women in our series were older on average (70 years vs 67 years), but the reason for the reversal of late survival results is not apparent.

Diabetes was an important predictor because patients with diabetes had significantly shorter 5- and 7-year survival rates compared with those who did not (32.5% ± 5.5% and 28.2% ± 5.5% vs 54.2% ± 4.4% and 39.1% ±5.1%, respectively). Diabetes would be expected to be an important factor because it is associated with diffuse atherosclerosis as well as the presence of comorbid medical disease.[26]

Our patients who had renal insufficiency had a significantly lower 5- and 7-year survival rates than those who had normal renal function (20.6% ± 8.6% and 7.7% ± 6.7% vs 49.9% ± 3.7% and 38.3% ± 4.2%, respectively). To create a categoric variable, renal insufficiency was defined as an abnormal creatinine level greater than 1.7 mg/dl or 150 SI units, and the significant subgroup difference in survival rate at this cutpoint was unexpected. Of the 44 patients who had a creatinine level greater than 1.7 mg/dl or 150 SI units, only six were on dialysis (three hemodialysis and three peritoneal dialysis). In patients who had end-stage renal failure, the decreased long-term survival rate is not surprising. Sanchez et al.[27] reported that the 2-year survival rate was only 45.6% and recommended consideration of primary amputation in those patients who have unrelenting infection or mid-forefoot gangrene. The association of decreased late survival rate at lesser degrees of renal dysfunction is of potential value in patient selection, particularly if it coexists with other independent predictors.

A history of cerebrovascular disease predicts a lower survival rate (30.9% ± 7.1% and 20.6% ± 6.9% vs 51.6% ± 3.9% and 38.4% ± 4.5% at 5 and 7 years, respectively). That a patient has had symptomatic arterial disease in more than one vascular bed is a warning that diffuse atherosclerosis is present, and the patient is at higher risk for cardiac or cerebrovascular death. Even diffuse disease of the legs appears to be a predictor of lower survival rate. Kram and colleagues[19] reported that the presence of an isolated popliteal segment, which denotes diffuse tibial disease, is associated with limited life expectancy (38% at 5 years) because of associated coronary disease. Although by univariate analysis coronary artery disease

was significantly associated with late survival ($p < 0.004$), this variable was not retained in the multivariate model as an independent predictor because of the prevalence.

With the worst-case scenario-male gender, diabetes, chronic renal insufficiency (creatinine level greater than or equal to 1.7 mg/dl or 150 SI units) and a history of cerebrovascular disease-the predicted cumulative 5-year survival rate was 2%, compared with the best scenario (female gender, nondiabetic, normal renal function, no history of cerebrovascular disease), in which the cumulative 5-year survival rate was 71%. The survival rate was 43% to 60% when one variable was present, 23% to 42% when two variables were present, and 8% to 22% when three were present.

CONCLUSION

The results of this paper illustrate that certain preoperative variables are predictive of lower late survival rates after distal bypass surgery-male gender, diabetes, chronic renal insufficiency (creatinine level 1.7 mg/dl or 150 SI units or greater), and a history of cerebrovascular disease. If a patient has a poor chance of late survival and is not likely to obtain prompt and good functional recovery, an aggressive distal revascularization procedure might not be warranted, and the best palliation may be obtained by primary amputation.

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